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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/916,396	07/27/2001	Gregory M. Fahy	CENTMED.020A	7764

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EXAMINER	
SAUCIER, SANDRA E	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,396	FAHY, GREGORY M.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-10,13 and 15-32* is/are pending in the application.

4a) Of the above claim(s) *8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,10,13 and 15-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-4, 6-10, 13, 15-32 are pending. Claims 1-4, 6, 7, 10, 13, 15-32 are considered on the merits. Claims 8 and 9 are withdrawn from consideration as being drawn to a non-elected invention.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

NEW MATTER

Claims 7, 24, 25 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Insertion of "sucrose" in the claimed composition of claim 7 appears to be new matter. No mention of sucrose being included in the composition appears in the narrative portion of the specification, in the original claims or in any of the exemplified species.

Classification of polyglycerol, PVP, PVA, copolymer of vinyl alcohol and vinyl acetate as impermeants in claim 7 does not seem to be supported by the disclosure as filed. These compounds are referred to in the original claims 4 and 6 as cryoprotectants.

Claim 24 presents a new generic concept, that is the inclusion of equal concentrations of lactose and mannitol. First, "concentration" is not defined in the specification as molar concentrations, but rather may be based on weight/volume. Thus, the use of this unsupported insertion leads to the inability to determine the metes and bounds of the claim. Further, only the insertion of 45mM of each of lactose and mannitol are supported in the examples. This is not sufficient support for the recitation of equal

concentrations of lactose and mannitol as the relationship between the concentrations is not presented as a generic concept.

One is not free to expand the scope of the disclosure or to introduce new concepts during prosecution.

Please see *Gentry Gallery v. Berkline* 45 U.S.P.Q.2d 1498 for a discussion related to broadening the claimed invention without support in the as-filed specification. Please see *PurduePharma v. Faulding* 56 U.S.P.Q.2d 1481 for a discussion related to a failure to describe a claimed generic concept in the narrative portion of the specification, but rather basing support on limitations in examples.

INDEFINITE

Claim 24, 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"Concentration" is not defined in the specification as molar concentrations, thus, a reasonable, alternative interpretation may be based on weight/volume or weight/weight, all terms of concentration. Thus, the use of this unsupported insertion leads to the inability to determine the metes and bounds of the claim since an equal concentration may be interpreted to be three different types of measurement which would lead to three different amounts of each compound being the "same concentration" in claim 24.

Claims 27-29 use "X1000", DMSO, LM5. It is unclear what compounds are intended by these abbreviations. Are they tradenames or trademarks, if so they should be so identified. What exactly is encompassed by these undefined abbreviations?

Claim Rejections - 35 USC § 102

Claims 1, 2, 7 and 19 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by JP 1-106826 [L].

The claims are directed to a composition for the introduction and washout of vitrifiable concentration of cryoprotectants comprising: mannitol, lactose.

JP 1-106826 disclose a solution used for the preservation of red cells comprising mannitol, lactose with other sugars and sugar alcohols, see abstract.

Claim Rejections - 35 USC § 103

Claims 1-3, 10, 13, 15, 16, 19, 22-26, 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,194,137 [A10].

The claims are directed to a solution to be used in the treatment of cell, tissue or organ with cryoprotectants comprising:
1) mannitol,
2) lactose,
3) bicarbonate
4) glucose
5) vitrifiable concentrations of cryoprotectants, DMSO, EG, formamide.

US 6,194,137 discloses compositions for use in cryoprotection of cells and tissues comprising:
any combination of cryoprotectants sufficient for vitrification (col. 6, l. 22) such as lactose and glucose (col. 6, l. 41) and DMSO, EG and formamide (col. 6, l. 24) in a vehicle such as Euro-Collins or RPS-2 (col. 6, l. 66) which contains sodium bicarbonate and glucose (Table 1), and may include at least one osmotic buffering agent such as mannitol (col. 9, l. 27). The range of glucose used in the prior art reference is from 5-194mM, see tables. The concentrations of other components such as DMSO 24.2 w/w%, formamide 14.0 w/w%, Calcium chloride 1mM, magnesium chloride 2mM, glutathione 5mM, potassium

phosphate 7.2mM, 28,2mM potassium chloride, 1mM adenine, 10mM sodium bicarbonate tables 1-3.

Claims 4, 7, 17, 20, 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,194,137 [A10] as applied to claims 1-3, 10, 13, 15, 16, 19, 22-26, 30-32 above, and further in view of US 6,395,467 [E10].

The claims are directed to the inclusion of PVA type compounds in the solution.

US 6,395,467 discloses that PVA additives (1-2% PVA is demonstrated in the examples) are very useful for enhancing the performance of biological cryopreservation solutions (col. 9, l. 44). Acetol 3% is also added to such solutions.

The inclusion of PVA in the composition of US 6,194,137 would have been obvious because US 6,395,467 teaches that PVA enhances the performance of biological cryopreservation solutions and '137 states that the solution may contain any combination of cryoprotectants sufficient for vitrification.

Claims 6, 7, 18, 21, 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,194,137 [A10] as applied to claims 1-3, 10-12, 14-16, 19, 22, 23 above, and further in view of Klebe *et al.* [A12].

The claims are further directed to the inclusion of polyglycerol in the composition.

Klebe *et al.* disclose that decaglycerol has cryoprotective properties and has been used solutions as a cryoprotectant for cells in a range of 0.1-30%. (abstract and Table 1).

The inclusion of decaglycerol as a cryoprotective agent in the solution of US 6,194,137 would have been obvious because Klebe *et al.* teach that decaglycerol, which is a polyglycerol, has cryoprotective properties and '137 teaches that any combination of cryoprotectants may be used (col. 6, l. 23).

All components of the composition as claimed have been used in the prior art for the same purpose as the instant purpose.

It is well known that it is prima facie obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

It is well known in the art to optimize concentrations within prior art concentrations or through routine experimentation. Generally differences in concentration will not support the patentability of the subject matter unless there is evidence indicating such concentration is critical MPEP 2144.05 II.A.

Response to Arguments

Applicant argues that surprising effects are achieved through the combination of lactose and mannitol since the limited solubilities of both are overcome. According to the Merck Index, 1 gram of lactose is soluble in 5 grams of water. Thus, 20grams/100mls or a 20% solution (0.58M) is possible, which is much below the 45mM concentration of the examples. Applicant's arguments might be more persuasive if accompanied by evidence instead of mere assertions and the claims were limited to the evidenced concentrations.

Applicant argues that US '137 does not provide guidance on which of the many possible combinations to use and fails to disclose the unexpected

benefits of combining mannitol and lactose in a single solution. US '137 indeed does not teach that one combination of cryoprotectants over another combination provides better results. That is why the reference is applied in a 103 fashion as opposed to an anticipatory rejection. When arguing unexpected effects, the claims should be limited to that which produces the effect. See In re Lindner, 173 USPQ 356 (CCPA 1972) and In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983) which teach that the evidence of nonobviousness should be commensurate with the scope of the claims.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743. The normal work schedule for Examiner Saucier is 8:30AM to 5:00 PM Monday, Tuesday and 8:30 AM to noon on Wednesday.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Customer Service Desk at (703) 308-0197 or (703)-308-0198. The number of the Fax Center for the faxing of official papers is (703) 872-9306 or for after finals (703) 872-9307.

Sandra Saucier
Primary Examiner
Art Unit 1651
November 3, 2003